STUDIES IN MYASTHENIA GRAVIS: TECHNICAL CARE OF THE THYMECTOMY PATIENT*

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ALTHOUGH the relationship of structural alteration of the thymus gland and myasthenia gravis is still not established[1, 2], surgical extirpation of this gland as a therapeutic measure continues to undergo evaluation in selected cases[1, 3]. In a myasthenic patient this, or any type of major surgery, carries specific implications and risks different from those in any other group of patients. The selection of myasthenic patients for thymectomy has been the subject of many papers[1] and will not be dealt with in detail here. It is important to mention that recent experience indicates that thymomas associated with clinical myasthenia are malignant in an extremely high proportion of cases[2]. This evidence dictates thymectomy in these patients, without consideration of other factors.

Successful preoperative preparation, performance of surgery and postoperative care of the thymectomy patient are the results of team effort comparable in scope to techniques used in open heart surgery. This paper describes methods and procedures evolved at The Mount Sinai Hospital, New York City, for the technical care of the patient undergoing such surgery. These procedures have resulted in a safe, smooth, effective performance of a major surgical maneuver in an extremely brittle group of subjects.

Different phases of the total management will be described so that the contribution and roles of all personnel and equipment may be indicated. This experience covers a series of 14 thymectomies performed in the past year, of which six were thymomas.

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Preoperative Phase

Because of the nature of this disease, the myasthenic is emotionally involved more than most patients with chronic illness. Evaluation of drug dosage is partially absolute, but when a state of stress or trauma supervenes, the intelligent and conscious cooperation of the patient with his physicians is of utmost importance. Therefore every effort is made before operation to acquaint our patients with all of the discomforts, apparatus and surroundings they will encounter. This includes meeting with patients recently thymectomized, visits to the recovery room and interviews with the staff involved. The medical staff becomes acquainted with the patient and attempts to evaluate his or her ability to cooperate. All questions are answered, within the limits of the individual's capability of assessing such information. The patient is shown how to cough and breathe and is familiarized with the mechanical respiration equipment that he may require.

A preoperative medical profile is obtained with particular emphasis on multiple points.

1. Laboratory Data:
   - Chest x-ray including tomography
   - Electrocardiogram
   - Determination of vital capacity
   - Blood chemistries including carbon dioxide, blood urea nitrogen, and a complete coagulation study
   - General medical status
2. Selection of proper time for surgery:
   - Emotional preparedness
   - Post menstrual phase for premenopausal females.
   - Freedom from even the most minor respiratory infection, as a compromised respiratory tree is the commonest cause for postoperative difficulty. Operation is postponed if there is evidence of such infection.
3. Preoperative x-ray therapy:
   - Extensive experience with such therapy has been gathered by Keynes[4]. Ease of the subsequent surgery, with shrinkage of the thymus or thymoma, is reported. At times, we have encountered serious difficulties after radiotherapy, as follows:
     a) Development of variability of response to cholinergic drug therapy, with a narrowing, and even inversion, of the therapeutic index[1].
     b) Complete unresponsiveness to cholingeric drugs with development of myasthenic crisis.

c) Radiation pneumonitis.

d) Surgical technique may not be facilitated by preradiation because of the residual increased vascularity of mediastinal structures.

e) Histologic evidence suggests that only the thymocytic (lymphocytic) element of the thymus is sensitive to x-ray exposure. These cells appear to have neither malignant nor "myasthenic" potential, which properties are related to the thymic epithelial cell. The latter is highly radio-resistant, even to supervoltage therapy[1, 2].

4. Preoperative adjustment of drug therapy:

No attempt is made to treat the patient with parenteral therapy until the morning of surgery. For several days prior to operation, cholinergic drug control is maintained only at levels compatible with comfort, with no effort made to achieve scrupulously optimal levels of muscular strength. Oral dosages thus arrived at are translated into the equivalent parenteral dosage[1] which is administered at a time calculated to be effective through the period of anesthesia induction. No supplementary cholinergic medication is given during surgery.

Technique of Anesthesia

Premedication consists of either meperidine (Demerol) alone or in combination with promethazine hydrochloride (Phenergan), given intramuscularly one hour before surgery. Atropine and scopolamine are avoided because of the thick secretions that follow their use and because these agents may mask overdose of cholinergic medication.

The neuromuscular and pulmonic aspects of the problem influence directly the choice of anesthetic agents and techniques. The nature of the procedure requires complete control of respiration. The anesthetic agent used must be capable of producing any level of anesthesia necessary, must be quickly eliminated, must provide for the inclusion of a high level of oxygenation, and should not require routine supplementation with muscle relaxants. The anesthetic of choice should not promote secretions or produce postoperative depression of the patient. The agent that most readily meets these criteria is cyclopropane. Following transtracheal cocainization with 2 ml. of 5 per cent cocaine, the patient is given a small dose of thiopental sodium intravenously. As soon as there is loss of consciousness, intubation is performed. Following the transtracheal cocainization, this procedure can usually be done without the use of muscle relaxants. Anesthesia is then continued with cyclopropane and oxygen. With proper assistance, controlled respiration is established

without difficulty. Only minimal amounts of cyclopropane are required. In the few patients in whom a muscle relaxant is necessary, the agent of choice is succinylcholine. All relaxants in the non-depolarizing group are absolutely contraindicated (curare as d-tubocurarine, gallamine and mytolon)[5]. Control of ventilation may be accomplished manually by means of a mechanical device, depending upon the preference of the anesthetist. Inasmuch as copious amounts of secretions may be produced suddenly, frequent tracheobronchial aspirations are necessary, and this may prove to be the most difficult part of the anesthesia.

A very light plane of anesthesia is needed, with adequate ventilatory exchange being the important feature so that there is no retention of carbon dioxide or bronchial secretions.

Rarely, a patient may be encountered who, in addition to myasthenia, suffers from bronchial asthma. In this case the use of succinylcholine and nitrous oxide oxygen is safer than cyclopropane. If bronchospasm develops in such a subject, supplements of succinylcholine, helium and aminophylline are all of value. Because of its tendency to create a curariform type of neuromuscular block, as well as being capable of increasing bronchial secretions, ether is contraindicated for use as the anesthetic agent[6].

The tracheobronchial tree must be completely cleared before the patient leaves the operating room. Simple auscultation of the chest will help to determine this. A chest x-ray is done routinely upon arrival in the recovery room. If there is any question of adequacy of lung expansion, or should pneumothorax or atelectasis be suspected, the x-ray is taken before the patient is moved from the operating table.

It is most desirable that the patient be awake and have an active cough reflex before leaving the operating room.

Surgical Technique

A sternal splitting incision, carried in the skin from the jugular notch to the fourth intercostal space, is employed. The sternum is split longitudinally with due regard for the length of the incision and then is severed laterally into the interspace. Upon insertion of a self-retaining retractor, excellent exposure of the thymus is obtained over its entire length and breadth. Such exposure, as well as the good chest wall stability afforded during the postoperative phase, makes this approach most satisfactory.

In patients without thymoma, the bilobed, delicately encapsulated thymus is readily evident, lying in the loose areolar tissue of the anterior mediastinum. The two lateral thymic lobes may extend from the lower poles of the thyroid superiorly to overlie the pericardium inferiorly. They border on the phrenic nerves and particularly the left innominate vein, which at times may be completely surrounded.

In non-tumescent cases the gland is almost always readily dissected free from its bed. The operative management of the tumescent gland represents a more complex technical problem. It should be pointed out that this tumor bears different criteria for malignancy than most neoplasms in that these criteria are gross rather than microscopic. In histologic section the characteristics of malignancy are notably absent in even the most blatantly invasive tumor. The malignancy of this neoplasm is indicated by capsular and local invasiveness as well as by separate pleural and percardial implants[2]. Such secondary deposits may be found in both pleural cavities; and further, because of their mediastinal location, may escape even the most careful preoperative x-ray evaluation. Therefore the following are recommended:

a) Obligatory total thymectomy, rather than thymomectomy, in cases where the tumor is localized to one lobe.
b) Removal *en bloc* of any contiguous adherent structures that may safely be sacrificed.

In view of these facts, surgical management of the thymoma patient varies from case to case, depending upon the extent of the tumor. In practice, following the initial sternal splitting incision, the mediastinal pleura is opened widely, bilaterally, so that relation of the phrenic nerves to the tumor and the presence of any implants may be gauged. The tumor and any contiguous structure are then removed *en bloc*, including pericardium, pleura, innominate vein or any other tissues involved. In all cases a special attempt is made to preserve the phrenic nerves so that later respiratory excursions be affected as little as possible. The difficulty of the resection will, of necessity, be dependent on the degree of invasion found. Following extirpation of these tissues, the residual mediastinal structures are dissected free and cleared of any remaining fatty or lymphatic tissue.

In all cases, transpleural mediastinal drainage is obtained by means of intercostal chest tubes under water-seal suction. If neither pleural space has been entered during resection, the mediastinal pleura is opened

widely on one side to allow this drainage. Should both pleural spaces have been entered, bilateral chest tubes are used. Mediastinal collections of fluid, serum or blood have been avoided by such tubes and no problem has been occasioned by their presence even when the use of a Drinker respirator was required. In general, chest tubes may be removed within 48 to 72 hours.

An obligatory tracheostomy is performed in the operating room at the close of the procedure, as soon as adequate spontaneous respirations have become established. In order to avoid communication with the upper part of the mediastinal dissection and to facilitate care in a respirator, the tracheal stoma is placed as high as possible, usually through the first or second cartilaginous ring. Tracheostomy is performed before extubation. The largest caliber tracheal tube accepted is employed with an inflatable rubber cuff affixed to its exterior. Such a cuff prevents, if necessary, any regurgitation of air through the oro- and nasopharynx if the myasthenic's weak glottic closure is unable to cope with the stress developed by mechanical positive pressure respiratory assistance. Cuffing also allows only a minimum of oropharyngeal secretions to descend into the trachea, removing a possible source of bronchial aspiration. The tracheostomy tube is doubly secured by skin sutures so that no future manipulation of the patient may dislodge the airway.

Postoperative Care

When the surgical procedures are concluded and the patient displays forceful spontaneous respirations, transfer to a "complete care unit" is effected. Intensive, continuous observation for several days is afforded the patient, within a locale containing all possible equipment required for any eventuality.

Surgical aspects of the postoperative care have presented few problems and follow the accepted principles employed in any type of thoracic procedure. Antibiotics, replacement of blood loss, attention to reexpansion of the lungs are scrupulously attended to. Fluid requirements are given parenterally for a somewhat longer period than usual, in view of the dysphagia so common in this group of subjects. Enemas are contraindicated since deaths have been reported following the use of this procedure[7].

The care of the tracheobronchial tree is of paramount importance. The profuse secretions often encountered demand frequent, exacting

tracheal and oropharyngeal suctioning. However, care must be taken to keep these secretions moist and fluid. Cold steam, with or without bronchodilators, is used. Atropine is employed only when the secretions are inordinately profuse. If, despite these measures, atelectasis or inspissation of secretions occurs, free and repeated use of bronchoscopy is employed. Bronchorrhea may persist for some time and care is taken not to remove the tracheostomy tube prematurely.

Maintenance of Adequate Respiratory Exchange; Management of the Myasthenic State

These two phases of postoperative management are closely related and require the closest cooperation of surgeon, internist and anesthesiologist.

In contrast to previously reported experience[7], little difficulty in maintaining respiration has been encountered in the immediate postsurgical period, since most patients display a marked, if transitory, improvement in their myasthenic symptoms. Therefore, no supplementation of the preoperative cholinergic medication has been given. Such management is continued for the first several days, in that cholinergic drugs are given only to maintain respiration, with no attempt to titrate to optimal muscular strength. The initiation of even this minimal drug therapy usually is necessary only after the first 18 to 24 hours. The use of drugs in this fashion has obviated cholinergic crisis and has minimized the hypersecretion inherent in the use of cholinergic drugs. All medication of this type is given on a demand schedule, confirmed by Tensilon testing and clinical response[8]. Demand for cholinergic medication has been found to vary widely from patient to patient and even by the same patient, with time. Postoperatively there is little relationship to the preoperative dose requirement, and, in general, no empiric statement of dosage is possible. The intravenous route of drug administration permits the best and safest control. The drug of choice is Mestinon bromide (pyridostigmine bromide). Not until oral feedings are tolerated can cholinergic drugs be given *per os*, because absorption from an empty gastrointestional tract is erratic and unreliable. This time coincides, in most patients, with a return of stability of the myasthenic state so that routine medication may be given.

The pain caused by the incision, chest tubes and bandages, when coupled with the muscular weakness of the patient, may not allow ade-

quate ventilation even with cholinergic medication. In such cases intermittent respiration assistance must be supplied. Occasionally this may be required at the conclusion of surgery. The Bird Residual Breather MK7 has proved eminently satisfactory. This device is a pressure-cycled ventilator which is either automatic or patient-triggered. If the patient fails to breathe within a predetermined interval, the machine can be adjusted to cycle automatically and inflate the lungs. A nebulizer is incorporated in the circuit. Adjustment is possible to control the amount of positive pressure, the duration of the inspiratory phase, the rate of ventilation and the degree of sensitivity of response to any attempt by the patient to initiate respiration. The length of the expiratory phase may also be preset and there is provision for manual control. This machine's great versatility, its ease of operation and the favorable comments of patients who had previous experience with other devices, have impressed us with its performance. However, in case of atelectasis or tracheal plugging, the Drinker respirator is superior in permitting better gas exchange, although not allowing the same nursing care or the same physical and psychological freedom for the patient. It is pertinent to mention that should intermittent positive pressure assistance be necessary, close attention must be paid to the total time during which the endotracheal cuff is inflated. If this time is too prolonged, necrosis of the tracheal wall may ensue. A far preferable course in such instances is the use of the Drinker respirator.

Narcotics (meperidine) and sedative drugs (promethazine hydrochloride and its derivatives, and phenobarbital) are used in minimal amounts. They need not and should not be withheld because of the myasthenic state.

A partial listing of general complications encountered and dealt with include: respiratory acidosis, carbon dioxide narcosis with delirium, hyperthermic states, loculated effusions and paroxysmal tachycardia. A specific complication is the peculiar addiction to respiratory assistance evidenced by some patients, even when they are demonstrably capable of good spontaneous ventilation. Because of this, only the briefest possible use of mechanical assistance is desirable.

Successful resolution of these and other postoperative complications has depended primarily upon the closest of observation and harmonious cooperation of the associated medical personnel, including superior nursing team care.

Continued convalescence takes place on a ward or private room basis after complete stabilization. Return to preoperative quarters has usually been possible on the fifth postoperative day.

Summary

Experience with 14 selected myasthenic patients undergoing thymectomy during the past year has led to the adoption of procedures which have been most satisfactory.

Cooperation of surgeon, anesthesiologist and internist, coupled with care of the patient in suitable surroundings, has permitted smooth performance of major surgery in a difficult situation. The contribution of each specialist is analyzed in terms of the particular problems presented by the myasthenic undergoing thoracic surgery. Discussion of total thymectomy is presented concerning preoperative, anesthetic, surgical and postoperative phases of management. Methods of choice are presented in each of these disciplines. The malignant potential of thymoma associated with myasthenia gravis makes surgery mandatory in these patients.

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